

Attorney Docket No. 5219US
Serial No. 09/888,824REMARKS/ARGUMENTSRECEIVED
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Claims 70, 72-78, 82-86, 91, 96 and 98-102 are pending in the present application. Claims 101 and 102 have been withdrawn from consideration. Claim 73 was objected to as being improperly amended. Proper amendment has been made herein. Claims 74 and 75, being dependent upon claim 73 were also objected to, but the corrected amended version of claim 73 is considered to also address these objections.

In the office action, claims 70, 72, 76, 78, 82, 84-86, 96, and 98-100 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Comai et al (U.S. Patent No. 4,218,443) in view of Muller et al (U.S. Patent No. 6,783,949), the NEFA-C kit from Wako, and Wang et al (J. Lipid Res (1993) 34:2091). This rejection is respectfully traversed.

Comai relates to the use of polyether ionophores as anti-obesity and hypotriglyceridemic agents in warm blooded animals. These agents are administered orally to the animals. Within Comai, the disclosed anti-obesity and hypotriglyceridemic effects are confirmed by a variety of tests to show *in vitro* and *in vivo* inhibition of pancreatic lipase, lipoprotein lipase, fatty acid synthesis and measurements of decreased body fat and serum triglycerides (see col. 17, lines 18-22 of Comai). The methodology for confirming the inhibition of lipoprotein lipase is found within Example 3 of Comai. As admitted in the office action, the methodology described in Comai does not teach an enzymatic release of fatty acids or the addition of a colipase.

Muller relates to processes for determining whether a test substance contains lipases or lipase inhibitors which utilize a fluorescent label. It is true that Muller generally states that the activity of lipolytic enzymes is traditionally investigated using radiometric, titrimetric, enzymatic, or fluorimetric/photometric methods, and that Muller recites certain disadvantages to the use of radiometric assays, including the need to dispose of radioactive waste. However, Muller also recites certain disadvantages associated with the use of enzymatic or chromatographic methods. Specifically, Muller acknowledges that they are complicated in terms of handling and that when investigating unknown substances (*e.g. searching for potential inhibitors*), an effect on

the enzymes of the detection reaction cannot be excluded and require appropriate controls (see col. 1, line 66 to col. 2, line 10 of Muller). Muller teaches that these disadvantages gave the impetus to the development of fluorimetric/photometric processes (see col 2, lines 11-12 of Muller). Thus, Muller clearly teaches away from the use of an enzymatic method of measuring the release of free fatty acids from lipolysis, especially with unknown substances.

There is no motivation for a person skilled in the art at the time of the present invention to combine the cited references or modify the references. The disclosure of Comai is directed to specific orally administered compounds with anti-obesity and hypotriglyceridemic effects. The assay described in Comai merely shows an inhibitory effect of LPL by these specific compounds (e.g., the ionophores), which in turn is provided as indicative of the claimed anti-obesity and hypoglycemic effects, and is not taught to be a screening methodology for a variety of compounds that may be utilized in the manufacture of topical compositions for inhibiting LPL. In contrast to the assertions in the office action, Muller, in fact, teaches away from the use of an enzymatic methodology, and thus even if, in arguendo, a skilled person would use the teaching of Muller in combination with the Comai assay, such as skilled person would be motivated to use a fluorimetric/photometric process, NOT an enzymatic process which is discussed by Muller as having disadvantages that the use of fluorimetric/photometric processes can overcome.

The NEFA-C kit from Wako is a commercial reagent kit employing acyl-CoA synthetase, acyl CoA oxidase and peroxidase. However, due to the disadvantages of enzymatic methods in the investigation of unknown substances for detecting products of lipolytic reactions, one skilled in the art would not be motivated to combine the NEFA-C kit with the assay of Comai in a screening method to identify compounds or extracts for manufacturing a topical composition for inhibiting LPL.

With regard to Wang, even if, in arguendo, Wang discloses the combination of apoC-II colipase and BSA causes a shift of LPL longer chain triglyceride substances, there is still no motivation to combine this teaching with the Comai assay. The mere fact that apoC-II colipase could be added to the Comai assay does not necessarily mean that one skilled in the art would be motivated to do so. The Comai assay, unchanged,

Attorney Docket No. 5219US
Serial No. 09/888,824

was capable of demonstrating the inhibition of LPL by the ionophores described in Comai. In fact, it was capable of demonstrating "significant inhibition" of the LPL. There is no motivation for one skilled in the art at the time of the invention to further add apoC-II colipase to the assay of Comai merely because it would act synergistically with the BSA and long chain triglycerides present in Comai to optimize assay conditions as there is indication that the assay of Comai required any optimization. The art must suggest the desirability of the modification for one of ordinary skill in the art at the time the invention was made.

Thus, Applicant respectfully submits that there is no showing of the teaching or motivation for a skilled artisan to combine the cited prior art references as asserted in the office action.


Also in the office action, claims 70, 72, 76-78, 82-86, 96, and 98-100 were rejected under 35 U.S.C. §103(a) as being unpatentable over Comai in view of Muller, the NEFA-C kit, and Wang, in further view of Vanio et al. This rejection is also respectfully traversed. The combination of Comai, Muller, the NEFA-C kit and Wang are discussed in detail above. As one skilled in the art would not be motivated to combine these references or modify the references for the reasoning discussed, one skilled in the art would not be further motivated to include Vanio within this combination to arrive at the presently claimed invention.

In the office action, claims 70, 72-78, 82-86, 96, and 98-100 were rejected under 35 U.S.C. §103(a) as being unpatentable over Comai, in view of Muller, the NEFA-C kit, Wang, and Vanio, in further view of Kobayashi (U.S. Patent No. 3,875,007). This rejection is also respectfully traversed. The combination of Comai, Muller, the NEFA-C kit, Wang, and Vanio are discussed in detail above. As one skilled in the art would not be motivated to combine these references or modify these references for the reasoning discussed, one skilled in the art would not be further motivated to include Kobayashi within this combination to arrive at the presently claimed invention.

Attorney Docket No. 5219US
Serial No. 09/888,824

Thus, for the reasons set out above, Applicants believe the present invention to be non-obvious over the cited art. Favorable consideration of this application, as amended, is respectfully requested.

Respectfully submitted,
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